

IN THE CLAIMS:

Please cancel claim 188 and add new claims 433-476 as shown below.

1-187. (Previously cancelled)

188. (Currently cancelled)

189-432. (Previously cancelled)

433. (New) A universal nanoparticle detection probe comprising (i) a nanoparticle; (ii) at least one type of oligonucleotides bound to the nanoparticle; and (iii) at least one type of binding oligonucleotides that is hybridized to at least a portion of at least one type of oligonucleotides, wherein each type of binding oligonucleotides has a sequence comprising at least first and second portions, wherein the first portion is complementary to at least a portion of the sequence of at least one type of oligonucleotides bound to the nanoparticles and the second portion is complementary to at least a portion of a sequence of a selected target nucleic acid.

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434. (New) The nanoparticle probe of Claim 433 wherein nanoparticle probe comprises one type of oligonucleotides.

435. (New) The nanoparticle probe of Claim 433 wherein the nanoparticle probe comprises two or more types of oligonucleotides.

436. (New) The nanoparticle probe of Claim 433 wherein the nanoparticle probe comprises one type of binding oligonucleotides.

437. (New) The nanoparticle probe of Claim 433 wherein the nanoparticle probe comprises two or more types of binding oligonucleotides.

438. (New) The nanoparticle probe of Claim 433 wherein each type of binding oligonucleotides have the same first portion and different second portions to bind to multiple portions of the target nucleic acid or to different target nucleic acids.

439. (New) The nanoparticle probe of Claim 433 wherein each type of binding oligonucleotides have a first portion that is complementary to a portion of a sequence of a specific type of oligonucleotides and a second portion that binds to a different portion of a selected target nucleic acid or to a different target nucleic acid.

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440. (New) The nanoparticle probe of Claim 433 wherein the oligonucleotides are attached to the nanoparticles in a stepwise ageing process comprising (i) contacting the oligonucleotides with the nanoparticles in a first aqueous solution for a period of time sufficient to allow some of the oligonucleotides to bind to the nanoparticles; (ii) adding at least one salt to the first aqueous solution to create a second aqueous solution; and (iii) contacting the oligonucleotides and nanoparticles in the second aqueous solution for an additional period of time to enable additional oligonucleotides to bind to the nanoparticles.

441. (New) The nanoparticle probe of Claim 440 wherein the second aqueous solution has an ionic strength sufficient to overcome at least partially the electrostatic attraction or repulsion of the oligonucleotides for the nanoparticles and the electrostatic repulsion of the oligonucleotides to each other.

442. (New) The nanoparticle probe of Claim 440 wherein the oligonucleotides are present on a surface of the nanoparticles at a surface density of at least 10 picomoles/cm².

443. (New) The nanoparticle probe of Claim 442 wherein the oligonucleotides are present on the surface of the nanoparticles at a surface density of at least 15 picomoles/cm².

444. (New) The nanoparticle probe of Claim 443 wherein the oligonucleotides are present on the surface of the nanoparticles at a surface density from about 15 picomoles/cm² to about 40 picomoles/cm².

445. (New) The nanoparticle probe of Claim 440 wherein the nanoparticles are metal nanoparticles or semiconductor nanoparticles.

446. (New) The nanoparticle probe of Claim 445 wherein the nanoparticles are gold nanoparticles.

447. (New) The nanoparticle probe of Claim 433 wherein the target nucleic acid is viral RNA or DNA.

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448. (New) The nanoparticle probe of Claim 433 wherein the target nucleic acid is a gene associated with a disease.

449. (New) The nanoparticle probe of Claim 433 wherein the target nucleic acid is a bacterial DNA.

450. (New) The nanoparticle probe of Claim 433 wherein the target nucleic acid is a fungal DNA.

451. (New) The nanoparticle probe of Claim 433 wherein the target nucleic acid is a synthetic DNA, a synthetic RNA, a structurally-modified natural or synthetic RNA, or a structurally-modified natural or synthetic DNA.

452. (New) The nanoparticle probe of Claim 433 wherein the target nucleic acid is from a biological source.

453. (New) The nanoparticle probe of Claim 433 wherein the target nucleic acid is a product of a polymerase chain reaction amplification.

454. (New) The nanoparticle probe of Claim 440 wherein at least some of the oligonucleotides on the nanoparticles comprise at least one type of recognition oligonucleotides, each type of recognition oligonucleotides comprising a spacer portion and a recognition portion, the spacer portion being designed so that it is bound to the nanoparticles, the recognition portion having a sequence complementary to at least a portion of a sequence of a selected type of binding oligonucleotides.

455. (New) The nanoparticle probe of Claim 454 wherein the spacer portion has a moiety covalently bound to it, the moiety comprising a functional group through which the spacer portion is bound to the nanoparticles.

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456. (New) The nanoparticle probe of Claim 454 wherein the spacer portion comprises at least about 10 nucleotides.

457. (New) The nanoparticle probe of Claim 456 wherein the spacer portion comprises from about 10 to about 30 nucleotides.

458. (New) The nanoparticle probe of Claim 454 wherein the bases of the nucleotides of the spacer portion are all adenines, all thymines, all cytosines, all uracils or all guanines.

459. (New) The nanoparticle probe of Claim 440 wherein at least some the oligonucleotides bound to the nanoparticles comprise at least one type of recognition oligonucleotides, each type of recognition oligonucleotides comprising a sequence complementary to at least one portion of a sequence of a selected type of binding oligonucleotides; and a type of diluent oligonucleotides.

460. (New) The nanoparticle probe of Claim 459 wherein, each type of recognition oligonucleotides comprises a spacer portion and a recognition portion, the spacer portion being designed so that it is bound to the nanoparticles, the recognition portion having a sequence complementary to at least one portion of a sequence of a selected type of binding oligonucleotides.

461. (New) The nanoparticle probe of Claim 460 wherein the spacer portion has a moiety covalently bound to it, the moiety comprising a functional group through which the spacer portion is bound to the nanoparticles.

462. (New) The nanoparticle probe of Claim 460 wherein the spacer portion comprises at least about 10 nucleotides.

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WD. 463. (New) The nanoparticle probe of Claim 462 wherein the spacer portion comprises from about 10 to about 30 nucleotides.

464. (New) The nanoparticle probe of Claim 460 wherein the bases of the nucleotides of the spacer portion are all adenines, all thymines, all cytosines, all uracils or all guanines.

465. (New) The nanoparticle probe of Claim 460 wherein the diluent oligonucleotides contain about the same number of nucleotides as are contained in the spacer portions of the recognition oligonucleotides.

466. (New) The nanoparticle probe of Claim 465 wherein the sequence of the diluent oligonucleotides is the same as that of the spacer portions of the recognition oligonucleotides.

467. (New) The nanoparticle probe of Claim 440 wherein the oligonucleotides and nanoparticles are contacted in aqueous solution for about 12 to about 24 hours.

468. (New) The nanoparticle probe of Claim 440 wherein salt is added to the aqueous solution to form the aqueous salt solution which is buffered at pH 7.0 and which contains about 0.1 M NaCl.

469. (New) The nanoparticle probe of Claim 440 wherein the oligonucleotides and nanoparticles are contacted in the aqueous salt solution for an additional 40 hours to increase the density of oligonucleotides bound to the nanoparticles.

470. (New) The nanoparticle probe of Claim 468 wherein the salt is added to the first aqueous solution in a single addition.

471. (New) The nanoparticle probe of Claim 465 wherein the salt is added gradually to the first aqueous solution over time.

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472. (New) The nanoparticle probe of Claim 465 wherein the salt is selected from the group consisting of consisting of sodium chloride, magnesium chloride, potassium chloride, ammonium chloride, sodium acetate, ammonium acetate, a combination of two or more of these salts, one of these salts in a phosphate buffer, and a combination of two or more these salts in a phosphate buffer.

473. (New) The nanoparticle probe of Claim 472 wherein the salt is sodium chloride in a phosphate buffer.

474. (New) The nanoparticle probe of Claim 433 wherein the presence of target nucleic acid and under hybridization conditions, the nanoparticle probe forms a complex with the target nucleic acid, the resulting nanoparticle-target nucleic acid complex having a sharp melting profile and increased melting temperature relative to a comparable complex without nanoparticles to allow for selective discrimination of any nucleotide insertion, deletion or mismatch in the target nucleic acid.

475. (New) The nanoparticle probe of any one of Claims 433, 440, 454, or 459 wherein the oligonucleotides are bound to the nanoparticles through sulfur linkages.

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Q7. 476. (New) A kit for the detection of the presence or absence of a target nucleic acid comprising the nanoparticle probe of any one of Claims 433, 440, 454 or 459.
